FILE 'REGISTRY' ENTERED AT 09:48:39 ON 07 SEP 2004

=> S FACTOR VIII/CN
L1 3 FACTOR VIII/CN

=> D 1-3

L1 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 113189-02-9 REGISTRY
CN Blood-coagulation factor VIII, procoagulant (9CI) (CA INDEX NAME)
OTHER NAMES:
CN AHF-A
CN Antihemophilic factor
CN Antihemophilic factor A
CN Antihemophilic globulin
CN Bioclate
CN Blood-coagulation factor VIII
CN Blood-coagulation factor VIIIc
CN Coagulation factor VIIIc
CN **Factor VIII**
CN Koate DVI
CN Monoclate
CN Monoclate-P
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CBNB, CEN, CIN, DIOGENES, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MSDS-OHS, PHAR, PIRA, PROMT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1838 REFERENCES IN FILE CA (1907 TO DATE)
45 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1845 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 109319-16-6 REGISTRY
CN Blood-coagulation factor VIII, von Willebrand's (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigens, blood-coagulation factor VIII-related
CN Blood platelet-aggregating factor
CN Blood-coagulation factor VIII
CN Blood-coagulation factor VIII antigen
CN Blood-coagulation factor VIII-related antigen
CN Blood-coagulation factor VIIIR

CN **Factor VIII**
CN Ristocetin cofactor
CN Ristocetin-von Willebrand factor
CN von Willebrand's factor
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, DIOGENES, EMBASE, IPA, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3966 REFERENCES IN FILE CA (1907 TO DATE)
75 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3977 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 9001-27-8 REGISTRY
CN Blood-coagulation factor VIII, complex (9CI) (CA INDEX NAME)
OTHER NAMES:
CN AHF
CN AHF-HP
CN AHG
CN Amofil
CN Beriate HS
CN Biostate P
CN Blood-coagulation factor VIII
CN **Factor VIII**
CN Factorate
CN Fanhdi
CN FVIII-THP/SD
CN Haemate
CN Haemate HS
CN Haemate P
CN Haemoctin SDH
CN Hemate P
CN Hemofil
CN Hemofil M
CN Humafac
CN Humate P
CN Koate HP
CN Nordiocto
CN Octonativ-M7
CN Profilate

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CN   Thromboplastinogen
DR   9035-62-5, 114046-09-2
MF   Unspecified
CI   COM, MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CANCERLIT, CAPLUS, CBNB, CEN, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU,
       EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, PHAR,
       PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Book; Conference; Dissertation; Journal; Patent;
       Report
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       CMBI (Combinatorial study); FORM (Formation, nonpreparative); OCCU
       (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT
       (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P  Roles for non-specific derivatives from patents:  ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU
       (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT
       (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents:  ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            3668 REFERENCES IN FILE CA (1907 TO DATE)
              69 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            3670 REFERENCES IN FILE CAPLUS (1907 TO DATE)


FILE 'CAPLUS' ENTERED AT 09:49:27 ON 07 SEP 2004

=> S FACTOR VIII;S L1 OR L2
        850698 FACTOR
        753243 FACTORS
       1344376 FACTOR
                 (FACTOR OR FACTORS)
        100145 VIII
             5 VIIIS
        100147 VIII
                 (VIII OR VIIIS)
L2        7331 FACTOR VIII
                 (FACTOR(W)VIII)


         8783 L1
L3      10613 L1 OR L2

=> D SAVED
NAME             CREATED      NOTES/TITLE
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ABZYME/Q         11 FEB 2003  QUERY CREATED IN FILE CAPLUS


=> ACTIVATE ABZYME/Q
L4              QUE  ABB=ON  PLU=ON  ((CATALYSIS OR CATALYZES OR CATALYTIC OR C
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ATALYZED)(5A)ANTIBOD?) OR ABZYME

```
=> S L4
        171987 CATALYSIS
           415 CATALYSES
        172222 CATALYSIS
                 (CATALYSIS OR CATALYSES)
         32264 CATALYZES
        370402 CATALYTIC
            26 CATALYTICS
        370411 CATALYTIC
                 (CATALYTIC OR CATALYTICS)
        215837 CATALYZED
             1 CATALYZEDS
        215837 CATALYZED
                 (CATALYZED OR CATALYZEDS)
        413525 ANTIBOD?
          2184 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
           238 ABZYME
           147 ABZYMES
           283 ABZYME
                 (ABZYME OR ABZYMES)
L5        2209 ((CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?)
                OR ABZYME

=> S ALLO(W)ANTIBODY
          8152 ALLO
            63 ALLOS
          8214 ALLO
                 (ALLO OR ALLOS)
        266032 ANTIBODY
        305353 ANTIBODIES
        413484 ANTIBODY
                 (ANTIBODY OR ANTIBODIES)
L6          69 ALLO(W)ANTIBODY

=> S INHIBITOR
        450838 INHIBITOR
        469816 INHIBITORS
L7      725022 INHIBITOR
                 (INHIBITOR OR INHIBITORS)

=> S L6 AND L3;S L5 AND L3
L8           6 L6 AND L3


L9          13 L5 AND L3

=> S L8 OR L9
L10         17 L8 OR L9

=> D 1-17 CBIB ABS

L10  ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2004 ACS on STN
2004:160972   Document No. 141:145609  Extracorporeal adsorption of anti-
     factor VIII allo-antibodies on
     randomly functionalized polystyrene resins.  Huguet, Helene-Celine; Lasne,
     Dominique; Rothschild, Chantal; Siali, Rosa; Jozefonvicz, Jacqueline
     (Faculte des Sciences Pharmaceutiques, Universite Paris II, Chatenay
     Malabry, Fr.).  Thrombosis and Haemostasis, 91(2), 259-266 (English) 2004.
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CODEN: THHADQ. ISSN: 0340-6245. Publisher: Schattauer GmbH.

AB The occurrence of anti-**factor VIII** (FVIII) **allo-antibodies** is a severe complication of the treatment of hemophilia A patients, leading to the inhibition of transfused FVIII activity. The effective elimination of these inhibitory antibodies plays a decisive role in the management of affected patients. To achieve this, immunoadsorption devices employing synthetic adsorbers, which selectively eliminate inhibitors, are of interest in the treatment strategy of hemophilia A patients with inhibitors. Adsorbers consisting of polystyrene-based beads substituted with sulfonate and L-tyrosyl methylester groups, which mimic part of epitope of FVIII mol. recognized by inhibitors, exhibit selective binding capacities towards anti-FVIII antibodies. The adsorption of FVIII inhibitors was investigated by simulating an extracorporeal circulation of hemophilic plasma over these functionalized resins. These innovative adsorbers are able to remove around 25% of anti-FVIII antibodies in 15 min depending on the plasma tested. Furthermore, they do not modify the amount of essential plasmatic proteins or residual Igs G. Expts. which were carried out using different plasmas with various inhibitor titers demonstrate a good reproducibility regarding the adsorption capacity of the synthetic resin. The characteristics of adsorption are similar on either native or regenerated resins. Both the purely synthetic nature of the resin and its easy processability demonstrate the real advantages over currently available protocols. This synthetic adsorber is a major technol. advance in selective removal of FVIII inhibitory antibodies.

L10 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

2003:718895 Document No. 139:336549 **Catalytic antibodies** to **factor VIII** in haemophilia A. Lacroix-Desmazes, Sebastien; Kazatchkine, Michel D.; Kaveri, Srini V. (Institut des Cordeliers, INSERM U430, Paris, Fr.). Blood Coagulation & Fibrinolysis, 14(Suppl. 1), S31-S34 (English) 2003. CODEN: BLFIE7. ISSN: 0957-5235. Publisher: Lippincott Williams & Wilkins.

AB A review. The development of **factor VIII** (FVIII) inhibitors in haemophiliac patients following therapeutic administration of exogenous FVIII is one of the major factors complicating the treatment of this disease. Most FVIII inhibitors described to date appear to be directed towards epitopes involved in the procoagulant activity of FVIII. However, recent data suggest that some FVIII inhibitors may behave as **catalytic antibodies**, able to cleave FVIII by hydrolysis. This appears to be the first example of **catalytic antibodies** having a direct role in the etiol. of a disease. Further characterization of these **catalytic** anti-FVIII **antibodies** may lead to the identification of novel therapeutic approaches for the future management of FVIII inhibitor patients.

L10 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

2003:319446 Document No. 138:336413 Covalently reactive transition state analogs (CRTSA) of antibody for treating autoimmune, microbial, lymphoproliferative and neoplastic diseases and for screening phage display library and B cell-expressing surface antibody. Paul, Sudhir; Nishiyama, Yasuhiro (USA). U.S. Pat. Appl. Publ. US 2003078203 A1 20030424, 52 pp., Cont.-in-part of U.S. Ser. No. 862,849. (English). CODEN: USXXCO. APPLICATION: US 2002-114716 20020401. PRIORITY: US 1998-46373 19980323; US 2001-PV280624 20010331; US 2001-862849 20010522.

AB The CRTSA of **antibodies** or **catalytic antibodies** comprise an epitope of a target protein antigen, an electrophilic covalently reactive center bearing a partial or full neg. charge and an electron withdrawing (or donating) substituent optionally containing a flanking peptide sequence. The provided CRTSA are useful for production, selection and inhibition of **catalytic antibodies** specific to tumor necrosis factor, epidermal growth factor receptor, interleukin 1, gp120, gp160, gag, pol, HBsAg, bacterial exotoxin,

EGF, TGFα, p53, prostate-specific antigen, CEA, prolactin, hCG, c-myc, c-fos, c-jun, HER-2, prolactin receptor, steroid receptor and interleukin 4. The CRTSA antibodies are therefore useful as vaccine or for passive immunotherapy of autoimmune diseases, lymphoproliferative diseases, microbial infection,. The CRTSA antibodies are also useful for screening phage displaying or B cell expressing **catalytic antibodies** on the surface.

L10 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2003:250200 Document No. 139:4422 Hydrolytic activity of anti-F VIII antibody inhibitors in hemophilia A patients. Lacroix-Desmazes, Sebastien; Moreau, Alexandre; Bayry, Jagadeesh; Kazatchkine, Michel D.; Kaveri, Srinivas V. (Institut des Cordeliers, Inserm U. 430, Paris, 75006, Fr.). Hematologie, 8(6), 422-426 (French) 2002. CODEN: HEMAF2. ISSN: 1264-7527. Publisher: John Libbey Eurotext.

AB A review. Antibodies with hydrolytic activity have been described in human in several pathol. situations: lupus erythematosus, autoimmune thyroiditis, asthma and Bence-Jones disease. Although the target mols. hydrolyzed by the antibodies are self antigens (DNA, thyroglobulin, vasoactif intestinal peptide), a direct implication of the hydrolysis of the self-antigen in the etiol. of the disease has never been demonstrated. We have described the presence of IgG antibodies able to hydrolyze F VIII in patients with severe hemophilia A who have developed F VIII inhibitors following administration of therapeutic F VIII. The kinetic parameters of the clivage of F VIII by the anti-F VIII antibodies are in the range of that of **catalytic antibodies** previously described. We have further demonstrated that **catalytic antibodies** are present in more than 50% of inhibitor-pos. patients with severe hemophilia A. **Catalytic antibodies** to F VIII are the first example where the hydrolysis of the target mol. by proteolytic antibodies may be directly relevant to the etiol. of the disease. The identification of F VIII inhibitors as proteases will open the way to novel therapeutic approaches aimed at eliminating F VIII inhibitors in hemophilia A patients.

L10 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2003:168431 Document No. 138:395234 Autoantibodies to **factor VIII** with catalytic activity. Bayry, Jagadeesh; Lacroix-Desmazes, Sebastien; Pashov, Anastas; Stahl, Dorothea; Hoebeke, Johan; Kazatchkine, Michel D.; Kaveri, Srini V. (Institut National de la Sante et de la Recherche Medicale, Hopital Broussais, Paris, 75014, Fr.). Autoimmunity Reviews, 2(1), 30-35 (English) 2003. CODEN: ARUEBU. ISSN: 1568-9972. Publisher: Elsevier Science B.V..

AB A review. Hemophilia A is an X-linked, recessive, bleeding disorder caused by defective or deficient **factor VIII** (FVIII) mols. Infusion of purified FVIII to patients with severe hemophilia A results in approx. 25% of the cases, in the emergence of anti-FVIII antibodies (inhibitors) that are known to neutralize the pro-coagulant activity of FVIII by steric hindrance. We recently reported on the proteolysis of FVIII by **allo-antibodies** in the plasma of high responder patients with severe hemophilia A, demonstrating a new mechanism by which FVIII inhibitors may prevent the pro-coagulant function of FVIII. Hemophilia is the first model where a direct link between the hydrolysis of the target mol. and the occurrence of the clin. manifestations may be established. It also represents the first example in humans, of the induction of **catalytic antibodies** following the exogenous administration of an antigen. The characterization of FVIII inhibitors as site-specific proteases may provide new approaches to the treatment of inhibitors.

L10 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2002:787407 Document No. 138:37746 Antibodies with hydrolytic activity

towards **factor VIII** in patients with hemophilia A.
Lacroix-Desmazes, Sebastien; Misra, Namita; Bayry, Jagadeesh; Villard, Sylvie; Kazatchkine, Michel D.; Kaveri, Srinivas V. (Hopital Broussais, Institut National de la Sante et de la Recherche Medicale, Universite Pierre et Marie Curie, Paris, 75014, Fr.). Journal of Immunological Methods, 269(1-2), 251-256 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB Antibodies endowed with hydrolytic properties have been described in humans for over a decade in a variety of pathol. conditions such as systemic lupus erythematosus (SLE), autoimmune thyroiditis, asthma, and Bence Jones disease. Although the identified target substrate mols. have always been autoantigens (i.e., DNA, thyroglobulin, vasoactive intestinal peptide), a direct role of hydrolysis of the autoantigen in pathol. of the disease has not been clearly documented. We have described in multitransfused patients with hemophilia A the presence of anti- **factor VIII** (FVIII) IgG antibodies that hydrolyze FVIII. The estimated kinetic parameters derived for FVIII cleavage by anti-FVIII antibodies are in line with the previously described **catalytic antibodies**. The identified cleavage sites are evenly spread throughout the FVIII mol. and are located after an arginine or a lysine in most cases. We have recently shown that the **catalytic antibodies** are highly prevalent among hemophilia A patients with FVIII inhibitors. **Catalytic antibodies** to FVIII are the first example where the hydrolysis of the target mol. by hydrolytic antibodies may be directly relevant to the etiol. of the disease. The characterization of FVIII inhibitors as site-specific proteases may provide novel strategies in the design of therapy against FVIII inhibitors in patients with hemophilia A.

L10 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2002:220398 Document No. 136:252466 Injectable hybrid matrix mixtures.
Mineau-Hanschke, Rochelle; Lamsa, Justin Chace; Abalos-Coyle, Deborah (Transkaryotic Therapies, Inc., USA). PCT Int. Appl. WO 2002022157 A2 20020321, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US42085 20010910. PRIORITY: US 2000-662037 20000914.

AB The invention features a method of delivering a polypeptide to an animal. The method involves introducing into the animal a fluid mixture containing: a population of cultured vertebrate cells genetically engineered to express the polypeptide; and a plurality of microcarriers.

L10 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2001:78636 Document No. 134:146396 **Catalytic** anti-**factor VIII allo-antibodies**. Kaveri, Srinivas; Lacroix-Desmazes, Sebastien; Kazatchkine, Michel (Institut National de sa Sante et de la Recherche Medicale (INSERM), Fr.; Bayer Pharmaceuticals Corporation). PCT Int. Appl. WO 2001007918 A1 20010201, 36 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP6870

20000718. PRIORITY: EP 1999-401841 19990721.

AB The present invention relates to a method of determining the presence of **catalytic** anti-**factor VIII allo-antibodies** capable of degrading **Factor VIII** in a mammal, and of characterizing the cleavage sites in said **factor VIII** mol. by said **catalytic** anti-**factor VIII allo-antibodies**. It also relates to an anti-**factor VIII allo-antibody-catalyzed factor VIII** degradation inhibitor; and to a pharmaceutical composition comprising said **catalytic** anti- **Factor VIII allo-antibodies** which are capable of degrading **Factor VIII** and which originate from said method of determination; and further to a pharmaceutical composition comprising said anti-**factor VIII allo -antibody-catalyzed factor VIII** degradation inhibitor. Finally, the present invention relates to the application in therapeutics of said anti-**factor VIII allo-antibody-catalyzed factor VIII** degradation inhibitor, of a pharmaceutical composition comprising said **catalytic** anti-**factor VIII allo-antibodies** which are capable of degrading **factor VIII** and which originate from said method of determination, and of a pharmaceutical composition comprising said anti-**factor VIII allo-antibody-catalyzed factor VIII** degradation inhibitor.

L10 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

2000:903334 Document No. 135:91356 **Factor VIII** inhibitor with catalytic activity towards **factor VIII**. Lacroix-Desmazes, Sebastien; Sooryanarayana; Moreau, Alexandre; Kazatchkine, Michel D.; Kaveri, Srini V. (INSERM U430, Hopital Broussais, Paris, 75014, Fr.). Haematologica, 85(10, Suppl.), 89-92 (English) 2000. CODEN: HAEMAX. ISSN: 0390-6078. Publisher: Ferrata Storti Foundation.

AB Hemophilia A is an X chromosome-linked recessive disorder resulting in defective or deficient **factor VIII** (FVIII) mols., which, in its severe form, is a life-threatening, crippling hemorrhagic disease. Infusion of purified FVIII to patients with severe hemophilia A results in approx. 25% of the cases in the emergence of anti-FVIII antibodies (inhibitors) that are known to neutralize the procoagulant activity of FVIII by steric hindrance. We recently reported on the proteolysis of FVIII by alloantibodies in the plasma of two high responder patients with severe hemophilia A, demonstrating a new mechanism by which FVIII inhibitors may prevent the pro-coagulant function of FVIII. Hemophilia is the first model in which a direct link between the hydrolysis of the target mol. and the occurrence of clin. manifestations has been established. It also represents the first example in humans, of the induction of **catalytic antibodies** following the exogenous administration of an antigen.

L10 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

2000:738600 Document No. 134:324767 Immune tolerance therapy for haemophilia. Ho, Aloysius Y. L.; Height, Susan E.; Smith, Mark P. (The Haemophilia Reference Centre, St Thomas' Hospital, London, UK). Drugs, 60(3), 547-554 (English) 2000. CODEN: DRUGAY. ISSN: 0012-6667. Publisher: Adis International Ltd..

AB A review with 69 refs. The development of anti-**factor VIII** and anti-factor IX **allo-antibodies** in hemophilia A and B, resp., remains a serious complication of treatment for these two X-linked hemostatic disorders, with major clin. and economic consequences. Treatment of this potentially fatal complication remains one of the greatest challenges facing hematologists at the beginning of the 21st century. Immune tolerance induction (ITI) therapy has been generally accepted as the best available treatment, extinguishing the inhibitor and permitting a resumption of standard dosing schedules. Although there have been several established protocols for ITI therapy developed over

the last quarter century, the optimal scheme in terms of safety, clin. efficacy and pharmaco-economic considerations has yet to be determined

L10 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2000:716657 Document No. 134:96947 **Factor VIII** inhibitor with catalytic activity towards **factor VIII**.
Lacroix-Desmazes, Sebastien; Sooryanarayana; Moreau, Alexandre; Horn, Michel P.; Kazatchkine, Michel D.; Kaveri, Srini V. (INSERM U430, Hopital Broussais, Paris, Fr.). Chemical Immunology, 77(Catalytic Antibodies), 102-114 (English) 2000. CODEN: CHMIEP. ISSN: 1015-0145. Publisher: S. Karger AG.

AB A review with 38 refs. is presented regarding the **factor VIII** inhibitor with catalytic activity towards FVIII. Hemophilia A is an X chromosome-linked recessive disorder resulting in defective or deficient FVIII mol., which, in its severe form, is a life-threatening, crippling hemorrhagic disease. In approx. 25% of the cases, infusion of purified FVIII to patients with severe hemophilia A results in the emergence of anti-FVIII antibodies (inhibitors) that are known to neutralize the procoagulant activity of FVIII by steric hindrance. The proteolysis of FVIII by alloantibodies in the plasma of two high responder patients with severe hemophilia A, demonstrating a new mechanism by which FVIII inhibitors may prevent the procoagulant function of FVIII, has been recently reported. Hemophilia is the first model where a direct link between the hydrolysis of the target mol. and the occurrence of the clin. manifestations may be established. It also represents the first example in humans of the induction of **catalytic antibodies** following the exogenous administration of an antigen. The characterization of FVIII inhibitors as site-specific proteases may provide new approaches to the treatment of inhibitors.

L10 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2000:17626 Document No. 132:150422 Threonine-145/Methionine-145 variants of baculovirus produced recombinant ligand binding domain of GPIbα express HPA-2 epitopes and show equal binding of von Willebrand factor.
Li, Chester Q.; Garner, Stephen F.; Davies, Julian; Smethurst, Peter A.; Wardell, Mark R.; Ouwehand, Willem H. (Department of Hematology, National Blood Service East Anglia, University of Cambridge, Cambridge, CB2 2PT, UK). Blood, 95(1), 205-211 (English) 2000. CODEN: BLOOAW. ISSN: 0006-4971. Publisher: American Society of Hematology.

AB Glycoprotein (GP) Ibα is the functionally dominant subunit of the platelet GPIb-IX-V receptor complex, with the von Willebrand factor (vWF) binding site residing on the amino-terminus. A threonine for methionine-145 replacement of GPIbα is associated with the human platelet antigen (HPA)-2 system. To study the structural and functional consequences of this mutation, both forms of GPIbα were expressed as calmodulin fusion proteins in insect cells. Both recombinant proteins were recognized by their resp. alloantibodies, independent of glycosylation or intactness of disulfide bonds, and gave similar results to platelet-derived GPIbα in antibody detection assays. Resonant mirror studies showed that vWF binding was not affected by the HPA-2 mutation; however, vWF binding was partially inhibited by IgG HPA-2 antibodies. The data are compatible with an involvement of the leucine-rich repeat domain of GPIbα in vWF binding and indicate that recombinant GPIbα may be used to detect HPA-2 antibodies.

L10 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1999:708908 Document No. 131:318576 Delivery of **Factor VIII**, Factor IX, or other therapeutic proteins via implantation of

genetically modified cells in the omentum, and uses thereof in the treatment of coagulation and thrombosis disorders. Lamsa, Justin Chase; Treco, Douglas A. (Transkaryotic Therapies, Inc., USA). PCT Int. Appl. WO 9955866 A1 19991104, 55 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US8266 19990416. PRIORITY: US 1998-82982 19980424.

AB The invention provides a method of expressing therapeutic proteins, such as clotting factors, in a mammal by introducing a genetically modified cell into the omentum. The method of the invention allows for long-term systemic delivery of a protein of interest to a mammal for the prevention or treatment of disorders associated with coagulation and thrombosis. Preferably, the protein of interest is a **Factor VIII** or IX clotting factor, and thus, the invention provides methods and means for treating/preventing hemophilia.

L10 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

1999:575968 Document No. 131:306927 **Catalytic** activity of **antibodies** against **factor VIII** in patients with hemophilia A. Lacroix-Desmazes, Sebastien; Moreau, Alexandre; Sooryanarayana; Bonnemain, Cecile; Stieltjes, Natalie; Pashov, Anastas; Sultan, Yvette; Hoebeke, Johan; Kazatchkine, Michel D.; Kaveri, Srinivas V. (INSERM U430 and Universite Pierre et Marie Curie, Hopital Broussais, Paris, 75014, Fr.). Nature Medicine (New York), 5(9), 1044-1047 (English) 1999. CODEN: NAMEFI. ISSN: 1078-8956. Publisher: Nature America.

AB Hemophilia A is an X chromosome-linked recessive disorder resulting in defective or deficient **factor VIII** (FVIII) mols., which, in its severe form, is a life-threatening and crippling hemorrhagic disease. Infusion of homologous FVIII to patients with severe hemophilia A results, in 25% of patients, in the emergence of alloantibodies against FVIII (inhibitors) that inhibit FVIII procoagulant activity by steric hindrance of the interaction of FVIII either with stabilizing mols., with mols. essential for its activity or with activating mols. Here, we report on the proteolysis of FVIII by alloantibodies of two patients with severe hemophilia A, demonstrating a previously unknown mechanism by which FVIII inhibitors may prevent the pro-coagulant function of FVIII. The kinetic parameters of FVIII hydrolysis indicate a functional role for the catalytic immune response in the inactivation of FVIII in vivo. The characterization of alloantibodies against FVIII as site-specific proteases may provide new approaches to the treatment of FVIII inhibitors.

L10 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

1997:405951 Document No. 127:16498 Production of antibodies, and medical uses involving antibodies. Bradwell, Arthur Randell (Binding Site Limited, UK; Bradwell, Arthur Randell). PCT Int. Appl. WO 9717372 A1 19970515, 70 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-GB2638 19961030. PRIORITY: GB 1995-22554 19951103; GB 1996-15578 19960724.

AB A naive B-cell can be prevented from having a primary immunol. response to an antigen if antibodies to the antigen are already present. This can be exploited technol. by challenging an animal with unwanted antibodies, allowing it to produce desired antibodies that are more specific antibodies than has hitherto been possible. This enables better immunol. test kits to be produced. The feature of naive B-cell switch off can also be industrially applied to prevent an immunol. response to repeated administrations of physiol. active substances to a patient. The desire antibody is specific for antigen including streptokinase, TNF, selectin, cytokine, tumor targeting antibody, erythropoietin, **Factor VIII**, anti-botulism or diphtheria antiserum, antitoxin, or interferon.

L10 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1996:383310 Document No. 125:75045 Rationale and indications for continuous infusion of antihemophilic factor (**factor VIII**).
Goldsmith, J. C. (Alpha Therapeutic Corporation, Los Angeles, CA, 90032, USA). Blood Coagulation & Fibrinolysis, 7(Suppl. 1), S3-S6 (English) 1996. CODEN: BLFIE7. ISSN: 0957-5235. Publisher: Rapid Science Publishers.

AB A review with 9 refs. The continuous infusion of drugs and biol. compds., such as **factor VIII** concentrate, should enhance therapeutic efficacy. **Factor VIII** can be produced by recombinant DNA technol. or derived from plasma. Improvements to the stability of the compound have made continuous infusion feasible. Current and potential applications of continuous infusion of **factor VIII** product include (1) peri-operative conditions, (2) bleeding that threatens life or limb, (3) primary or secondary prophylaxis and (4) immune tolerance therapy for **factor VIII allo- antibodies.** Less use of costly **factor VIII** and decreased laboratory expenses also contribute to the usefulness of continuous infusion.

L10 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1996:58252 Document No. 124:78726 DNA construct for effecting homologous recombination and uses for recombinant protein production. Treco, Douglas A.; Heartlein, Michael W.; Selden, Richard F. (Transkaryotic Therapies, Inc., USA). PCT Int. Appl. WO 9531560 A1 19951123, 147 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US6045 19950511. PRIORITY: US 1994-243391 19940513.

AB The invention relates to constructs comprising: a) a targeting sequence; b) a regulatory sequence; c) an exon; and d) an unpaired splice-donor site. The invention further relates to a method of producing protein in vitro or in vivo comprising the homologous recombination of a construct as described above within the cell. The homologously recombinant cell is then maintained under conditions which will permit transcription and transition, resulting in protein expression. The present invention further relates to homologously recombinant cells, including primary, secondary, or immortalized vertebrate cells, methods of making the cells, methods of homologous recombination to produce fusion genes, methods of altering gene expression in the cells, and methods of making a protein in a cell employing the constructs of the invention.

=> S L6 NOT L10
L11 63 L6 NOT L10

=> D 1-63 TI

=> D 4,15,16,29-33,39,48,56 CBIB ABS

L11 ANSWER 4 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
2003:884126 Document No. 140:57960 The influence of pre-warming and warm-washing on the detection of IgG **allo-antibodies** in PEG-IAT tests. Straat, R. J. M. H. E.; Janse, T.; Beckers, E. A. M.; Berendes, P.; Sintnicolaas, K.; van Rhenen, D. J. (Regio Zuidwest Referentielaborratorium, Sanquin Bloedbank, Dordrecht, Neth.). Nederlands Tijdschrift voor Klinische Chemie en Laboratoriumgeneeskunde, 28(5), 275-279 (Dutch) 2003. CODEN: NTKCAS. ISSN: 1570-8306. Publisher: Nederlandse Vereniging voor Klinische Chemie.

AB Cold-reactive autoantibodies may interfere with the identification of IgG alloantibodies in the PEG-IAT. The use of pre-warmed testing is criticized because of the reported risk of failure of detecting clin. significant 37° antibodies. Instead, the use of BSA-IAT is advocated although it has a lesser sensitivity. This study was designed to evaluate the risk of non-detecting clin. significant antibodies in pre-warmed PEG-IAT tests and pre-warmed-warm-washed PEG-IAT tests compared to the routinely applied BSA-IAT. Of the total of 64 PEG-IAT reactive alloantibodies, all were reactive in the PEG-P (pre-warmed), 61 in the PEG-PW (pre-warmed-warm-washed) and only 41 in the BSA-IAT. The PEG-PW failed to identify 3 antibodies (1 anti-S; 2 anti-M). Two of these were also neg. in the BSA-IAT and 1 antiserum (anti-M) was only nonreactive in PEG-PW. Mean titer-scores of PEG-IAT, PEG-P, and PEG-PW for all antibodies tested were comparable. In contrast, only 8 of the 41 reactive BSA-IAT samples had comparable titer-scores, whereas the other 33 samples had lower titer-scores as compared to the PEG techniques. Thus, the fear of not detecting clin. important alloantibodies when using the PEG-P or PEG-PW is unjustified and should be lesser than the fear of not detecting alloantibodies in the BSA-IAT.

L11 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1999:330029 Document No. 130:324354 Detection of blood group antigens and alloantibodies. Frame, Thomas H.; Hatcher, David E.; Moulds, John J. (Gamma Biologicals, Inc., USA). U.S. US 5905028 A 19990518, 15 pp., Cont.-in-part of U.S. 5,665,558. (English). CODEN: USXXAM. APPLICATION: US 1996-728751 19961011. PRIORITY: US 1994-243296 19940517.

AB The authors disclose two methods, direct and indirect, useful for the detection of blood-group antigens and alloantibodies. The direct assay comprises adding a sample of erythrocytes to a reaction tube charged with two layers of particles. The first (upper) layer, preferably Sepharose, is coupled to Protein G; the second (lower) particle layer, preferably Sephacryl S-200, is coupled to Protein A. Antibodies specific for the blood-group antigens to be tested are liganded to the Protein G layer. The reaction tube is then centrifuged for a time sufficient to force to the bottom of the reaction tube erythrocytes that do not attach to the antibodies. The indirect assay comprises obtaining samples of erythrocytes, blood serum or blood plasma to be tested and mixing the erythrocytes, serum, or plasma with a known antibody or antigen reagent, depending on whether antigens or antibodies are being tested for. The mixture is incubated in a reaction tube as described above.

L11 ANSWER 16 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1998:128420 Document No. 128:216270 Agonistic and antagonistic interactions between CTLA4Ig and donor alloantigens in sensitized rat recipients of cardiac allografts. Onodera, K.; Chandraker, A.; Korom, S.; Stadlbauer, T. H. W.; Kato, K.; Kasai, S.; Sayegh, M. H.; Kupiec-Weglinski, J. W. (Harvard Medical School, The Surgical Research Laboratory, Department of Surgery, USA, and Medicine, Brigham and Women's Hospital, Boston, MA,

USA). Transplantation Proceedings, 30(1), 16-18 (English) 1998. CODEN: TRPPA8. ISSN: 0041-1345. Publisher: Elsevier Science Inc..

AB This study was designed to investigate the efficacy of and interactions between fusion protein CTLA4Ig and donor allo-Ag in a well-defined model of accelerated rejection of cardiac allograft (Tx) rejection in presensitized (with Brown Norway rat RT1n skin allograft) rat recipients. CTLA4Ig-mediated blockade of the CD28-B7 signaling pathway combined with transfusion of donor allo-Ag in the peritransplant period abrogated accelerated rejection and produced donor-specific tolerance in 33% of presensitized rat recipients, which was dose-dependent. The most effective CTLA4Ig-mediated blockade of the CD28-B7 signaling pathway in sensitized hosts requires adjunctive infusion of allo-Ag in a dose, which by itself enhances Tx survival. The question as to whether elevated **allo-antibody** levels (IgG or IgM) influence the host immune response by themselves, or their presence reflects the pattern of sensitization is still open.

L11 ANSWER 29 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

1992:19346 Document No. 116:19346 Detection of human monocyte-reactive alloantibodies by flow cytometry after selective downmodulation of the Fc receptor I. Kuijpers, R. W. A. M.; Dooren, M. C.; Von dem Borne, A. E. G. K.; Ouwehand, W. H. (Dep. Immunol. Haematol., Netherlands Red Cross Blood Transfus. Serv., Amsterdam, 1006 AK, Neth.). Blood, 78(8), 2150-6 (English) 1991. CODEN: BLOOAW. ISSN: 0006-4971.

AB Monocyte-reactive human alloantibodies may be of importance in situations such as transfusion reactions and bone marrow and kidney transplantation. So far, only complement-binding monocyte-reactive antibodies can be detected with a cytotoxicity assay. No antiglobulin assays are yet available that also detect noncomplement-fixing monocyte-reactive antibodies. The binding of monomeric IgG with high affinity to the Fc receptor I (FcRI) on monocytes has severely hampered the development of such an assay until now. The authors report on the selective removal of the FcRI from monocytes to test human sera in a flow cytofluorometry assay for the presence of monocyte-reactive IgG alloantibodies. Selective downmodulation of FcRI was accomplished by incubating the cells with murine monoclonal antibodies against FcRI followed by a second incubation with goat-antimouse IgG polyclonal antibodies. With such modified cells, human complement-binding and noncomplement-binding IgG and IgM alloantibodies against polymorphic determinants of the HLA class I and II glycoproteins, the human monocyte antigen system and polymorphic antigenic determinants of the LFA complex, can be detected in a sensitive and reproducible manner.

L11 ANSWER 30 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

1992:4884 Document No. 116:4884 Human monoclonal antibodies against blood group antigens preferentially express a VH4-21 variable region gene-associated epitope. Thompson, K. M.; Sutherland, J.; Barden, G.; Melamed, M. D.; Randen, I.; Natvig, J. B.; Pascual, V.; Capra, J. D.; Stevenson, F. K. (Dep. Biochem., Polytech. East London, London, E15 4LZ, UK). Scandinavian Journal of Immunology, 34(4), 509-18 (English) 1991. CODEN: SJIMAX. ISSN: 0300-9475.

AB An anti-idiotypic antibody has been raised which recognizes human Igs with cold agglutinin activity of anti-I/i specificity. The pattern of reactivity of the antibody indicates that the structural basis for the epitope is located in the VH4-21 gene segment of the VHIV family, which is preferentially utilized by these cold reactive antibodies. Using this antibody, epitope expression was investigated in a panel of 72 human monoclonal **allo-antibodies** specific for human blood group antigens, as compared with a control panel of 39 randomly selected human monoclonal IgM antibodies of unknown specificities. The anti-blood group panel included 44 IgM and 28 IgG monoclonal antibodies

against a variety of blood group antigens including the A antigen, Rh C, c, D, E, e, G antigens, and the Kidd antigens Jka and Jkb. The epitope was expressed by 64% (28/44) of the IgM anti-blood group antibodies and by 21% (6/28) of the IgG antibodies, but by only 7.7% (3/39) of the control IgM antibodies. Thus, the human alloimmune response to blood group antigens is biased in the use of VH gene families, with a preference for the VH4-21 gene segment of the VHIV family, or closely related gene segments. The fact that this mirrors the findings for the autoimmune cold agglutinins suggests a link in Ig gene usage between antibodies against structurally diverse antigens on the red cell surface.

L11 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1991:581264 Document No. 115:181264 Anti-HIV and anti-anti-MHC antibodies in alloimmune and autoimmune mice. Kion, Tracy A.; Hoffmann, Geoffrey W. (Dep. Microbiol., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.). Science (Washington, DC, United States), 253(5024), 1138-40 (English) 1991. CODEN: SCIEAS. ISSN: 0036-8075.

AB Alloimmune mice (mice that have been exposed to cells from another murine strain) were shown to make antibodies against gp120 and p24 of human immunodeficiency virus (HIV), and mice of the autoimmune strains MRL-lpr/lpr and MRL-+/+ made antibodies against gp120. This is surprising because the mice were not exposed to HIV. Furthermore, anti-anti-MHC antibodies (mols. that have shapes similar to those of major histocompatibility complex mols.) were detected in both alloimmune sera and MRL mice. These results are discussed in the context of a possible role for allogeneic stimuli in the pathogenesis of AIDS, as suggested by an idiotypic network model.

L11 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1991:581011 Document No. 115:181011 Heparin and platelet interactions influence alloantigen-induced proliferative responses of human T lymphocytes and immunoglobulin synthesis in vivo. Gorski, A.; Wasik, Maria; Stepien-Sopniewska, Barbara; Glapinski, T. (Transplantation INst., Warsaw Med. Sch., Warsaw, 02006, Pol.). Immunology Letters, 28(2), 161-5 (English) 1991. CODEN: IMLED6. ISSN: 0165-2478.

AB In contrast to defibrinated blood, cells isolated from heparinized blood give lower alloantigen-induced T-lymphoproliferative responses. Such responses can be also suppressed by addition of heparin to lymphocyte cultures. Platelets and heparin, combined, inhibited Ig production Platelets inhibit T cell proliferation and B cell differentiation, but their interactions with heparin may produce contrasting effects on different immune functions.

L11 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1991:183527 Document No. 114:183527 Intramolecular specificity of anti-HLA alloantibodies. Akkoc, Nurullah; Scornik, Juan C. (Coll. Med., Univ. Florida, Gainesville, FL, 32610-0275, USA). Human Immunology, 30(2), 91-8 (English) 1991. CODEN: HUIMDQ. ISSN: 0198-8859.

AB Recent descriptions of epitopes within HLA class I antigens recognized by mouse monoclonal antibodies are providing an antigenic map of such mols. However, for transplantation purposes, it is crucial to understand the epitope specificity of alloantibodies. To investigate this issue, sequential absorption/elution studies were performed with serum from a broadly sensitized patient and homozygous typing cells (HTCs) which shared one HLA-A,B antigen with the patient. Antibody reactivity in the different eluates was measured by flow cytometry in a panel of 20 HTCs. These studies revealed two major findings: (a) there were multiple antibodies recognizing one HLA antigen; for example, there were 8 anti-B62 antibodies, 8 anti-B51, 5 anti-B57, 5 anti-B46, and 4 anti-B35. (b) The reactivity of most antibodies correlated highly with

the presence of specific amino acids at a given position in the target HLA mol. Such residues were absent in most HLA antigens not recognized by the antibody. Most of the target residues were located in the accessible α helixes or connecting loops,but at least one antibody reactivity appeared to be influenced by residues located in the β sheets. The HLA antigens evaluated in this study were those of the B5, B15, B17 cross-reactive group which have multiple epitopic sites.

L11 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1980:507195 Document No. 93:107195 Reversible suppression of **allo-antibody** production by cyclosporin A. Denham, S.; Styles, J. M.; Barfoot, R. K.; Dean, C. J. (Div. Tumour Immunol., Chester Beatty Res. Inst., Sutton/Surrey, SM2 5PX, UK). International Archives of Allergy and Applied Immunology, 62(4), 453-8 (English) 1980. CODEN: IAAAAM. ISSN: 0020-5915.

AB Treatment of rats with 25 mg/kg/day of cyclosporin A (I) [59865-13-3] suppressed their immune response to skin allografts. Withdrawal of I treatment led to complete recovery of specific immune responsiveness and the time for recovery was independent of the duration of treatment. Titration of the dose of I administered in vivo indicated that doses of ≤12 mg/kg/day were not fully immunosuppressive.

L11 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1975:123107 Document No. 82:123107 Failure of pepsin digested donor specific alloantibody to prolong renal allograft survival in dogs. Callender, C. O.; Sutherland, D. E. R.; Howard, R. J.; Toledo-Pereyra, L. H.; Najarian, J. S. (Med. Sch., Univ. Minnesota, Minneapolis, MN, USA). Immunological Communications, 3(4), 309-19 (English) 1974. CODEN: IMLCAV. ISSN: 0090-0877.

AB Donor specific F(ab')2 alloantibody fragments, prepared by pepsin digestion of IgG from hyperimmune cytotoxic alloantiserums raised in third party dogs, was administered to canine renal alloraft recipients to allow expression of immunol. enhancing properties of alloantibody in a species in which hyperacute rejection occurred. Pepsin digestion did abrogate the ability of donor specific cytotoxic alloantibody to mediate hyperacute rejection, but renal allograft survival in F(ab')2 treated dogs was not prolonged over graft survival in untreated dogs. Factors which may contribute to the inability of this technique to prolong graft survival included the difficulty, when using outbred animals, of assuring that the alloantibody was directed against all the antigens present in the donor and absent in the recipient; and the decreased potency of F(ab')2 when compared to an equivalent amount of intact IgG, as an inhibitor of a specific immune response.

L11 ANSWER 56 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
1973:56361 Document No. 78:56361 Iodine-125-labeled rat transplantation alloantibody. I. Preparation. Shumak, K. H.; Batchelor, J. R.; Watts, H. G. (McIndoe Mem. Res. Unit, Queen Victoria Hosp., East Grinstead/Sussex, UK). Transplantation, 15(1), 70-9 (English) 1973. CODEN: TRPLAU. ISSN: 0041-1337.

AB Preparation of 125I-labeled AS anti-August rat transplantation alloantibody is described. After absorption and elution from membranes prepared from a spontaneous August myelogenous leukemia, antibody was partially purified on Sephadex G-200 and iodinated with 125I. After iodination, further purification was achieved by DEAE-cellulose chromatog. The final labeled preparation had a specificity ratio of 25-40:1 when the amount bound to August target lymphocytes was compared to that bound to AS target lymphocytes. The

specific binding activity could be absorbed by August cells and blocked by unlabeled antibody.

=> S L7 AND L6
L12 8 L7 AND L6

=> D 1-8 CBIB ABS

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
2004:442414 Antidotes to haemorrhage: recombinant factor VIIa. Kessler, Craig M. (Lombardi Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC, 20007, USA). Best Practice & Research, Clinical Haematology, 17(1), 183-197 (English) 2004. CODEN: BPRCA5. Publisher: Elsevier Science B.V..

AB Recombinant Factor VIIa (rFVIIa) concs. were originally developed to treat the refractory bleeding complications associated with **allo- antibody inhibitors** in hemophilias A and B. As experience was gained in the hemophilias, the physiol. of rFVIIa and its successes in controlling bleeds stimulated rFVIIa use in other challenging medical conditions complicated by bleeding. Thus, rFVIIa has assumed the role of a universal pancoagulant' without sufficient evidence-based data from well-designed, adequately powered clin. trials. This chapter discusses the anecdotal experience with rFVIIa based upon the few controlled trials that do exist, and emphasizes that these empirical dosing strategies have not yielded the best approach to achieve effective control of bleeding. Evidence-based data are necessary to establish the cost-benefit and risk-benefit profiles of rFVIIa, and to establish it as a standard treatment for bleeding.

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
2004:160972 Document No. 141:145609 Extracorporeal adsorption of anti-factor VIII **allo-antibodies** on randomly functionalized polystyrene resins. Huguet, Helene-Celine; Lasne, Dominique; Rothschild, Chantal; Siali, Rosa; Jozefonvicz, Jacqueline (Faculte des Sciences Pharmaceutiques, Universite Paris II, Chatenay Malabry, Fr.). Thrombosis and Haemostasis, 91(2), 259-266 (English) 2004. CODEN: THHADQ. ISSN: 0340-6245. Publisher: Schattauer GmbH.

AB The occurrence of anti-factor VIII (FVIII) **allo- antibodies** is a severe complication of the treatment of hemophilia A patients, leading to the inhibition of transfused FVIII activity. The effective elimination of these inhibitory antibodies plays a decisive role in the management of affected patients. To achieve this, immunoadsorption devices employing synthetic adsorbers, which selectively eliminate **inhibitors**, are of interest in the treatment strategy of hemophilia A patients with **inhibitors**. Adsorbers consisting of polystyrene-based beads substituted with sulfonate and L-tyrosyl methylester groups, which mimic part of epitope of FVIII mol. recognized by **inhibitors**, exhibit selective binding capacities towards anti-FVIII antibodies. The adsorption of FVIII **inhibitors** was investigated by simulating an extracorporeal circulation of hemophilic plasma over these functionalized resins. These innovative adsorbers are able to remove around 25% of anti-FVIII antibodies in 15 min depending on the plasma tested. Furthermore, they do not modify the amount of essential plasmatic proteins or residual Igs G. Expts. which were carried out using different plasmas with various **inhibitor** titers demonstrate a good reproducibility regarding the adsorption capacity of the synthetic resin. The characteristics of adsorption are similar on either native or regenerated resins. Both the purely synthetic nature of the resin and its easy processability demonstrate the real advantages over currently available protocols. This synthetic adsorber is a major technol. advance in selective removal of FVIII inhibitory antibodies.

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
2003:168431 Document No. 138:395234 Autoantibodies to factor VIII with catalytic activity. Bayry, Jagadeesh; Lacroix-Desmazes, Sebastien; Pashov, Anastas; Stahl, Dorothea; Hoebeke, Johan; Kazatchkine, Michel D.; Kaveri, Srini V. (Institut National de la Sante et de la Recherche Medicale, Hopital Broussais, Paris, 75014, Fr.). Autoimmunity Reviews, 2(1), 30-35 (English) 2003. CODEN: ARUEBU. ISSN: 1568-9972. Publisher: Elsevier Science B.V..

AB A review. Hemophilia A is an X-linked, recessive, bleeding disorder caused by defective or deficient factor VIII (FVIII) mols. Infusion of purified FVIII to patients with severe hemophilia A results in approx. 25% of the cases, in the emergence of anti-FVIII antibodies (**inhibitors**) that are known to neutralize the pro-coagulant activity of FVIII by steric hindrance. We recently reported on the proteolysis of FVIII by **allo-antibodies** in the plasma of high responder patients with severe hemophilia A, demonstrating a new mechanism by which FVIII **inhibitors** may prevent the pro-coagulant function of FVIII. Hemophilia is the first model where a direct link between the hydrolysis of the target mol. and the occurrence of the clin. manifestations may be established. It also represents the first example in humans, of the induction of catalytic antibodies following the exogenous administration of an antigen. The characterization of FVIII **inhibitors** as site-specific proteases may provide new approaches to the treatment of **inhibitors**.

L12 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
2002:102975 Document No. 136:379697 Calcineurin **inhibitor**-free CD28 blockade-based protocol protects allogeneic islets in nonhuman primates. Adams, Andrew B.; Shirasugi, Nozomu; Durham, Megan M.; Strobert, Elizabeth; Anderson, Dan; Rees, Phyllis; Cowan, Shannon; Xu, Huaying; Blinder, Yelena; Cheung, Michael; Hollenbaugh, Dianne; Kenyon, Norma S.; Pearson, Thomas C.; Larsen, Christian P. (Emory Transplant Center, Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA). Diabetes, 51(2), 265-270 (English) 2002. CODEN: DIAEAZ. ISSN: 0012-1797. Publisher: American Diabetes Association.

AB Recent success using a steroid-free immunosuppressive regimen has renewed enthusiasm for the use of islet transplantation to treat diabetes. Toxicities associated with the continued use of a calcineurin **inhibitor** may limit the wide-spread application of this therapy. Biol. agents that block key T-cell costimulatory signals, in particular the CD28 pathway, have demonstrated extraordinary promise in animal models. LEA29Y (BMS-224818), a mutant CTLA4-Ig mol. with increased binding activity, was evaluated for its potential to replace tacrolimus and protect allogeneic islets in a preclin. primate model. Animals received either the base immunosuppression regimen (rapamycin and anti-IL-2R monoclonal antibody [mAb]) or the base immunosuppression and LEA29Y. Animals receiving the LEA29Y/rapamycin/anti-IL-2R regimen (n = 5) had significantly prolonged islet allograft survival (204, 190, 216, 56, and >220 days). In contrast, those animals receiving the base regimen alone (n = 2) quickly rejected the transplanted islets at 1 wk (both at 7 days). The LEA29Y-based regimen prevented the priming of anti-donor T- and B-cell responses, as detected by interferon-γ enzyme-linked immunospot and **allo-antibody** production, resp. The results of this study suggest that LEA29Y is a potent immunosuppressant that can effectively prevent rejection in a steroid-free immunosuppressive protocol and produce marked prolongation of islet allograft survival in a preclin. model.

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
2001:78636 Document No. 134:146396 Catalytic anti-factor VIII **allo**

-**antibodies**. Kaveri, Srinivas; Lacroix-Desmazes, Sebastien; Kazatchkine, Michel (Institut National de sa Sante et de la Recherche Medicale (INSERM), Fr.; Bayer Pharmaceuticals Corporation). PCT Int. Appl. WO 2001007918 A1 20010201, 36 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP6870 20000718. PRIORITY: EP 1999-401841 19990721.

AB The present invention relates to a method of determining the presence of catalytic anti-factor VIII **allo-antibodies** capable of degrading Factor VIII in a mammal, and of characterizing the cleavage sites in said factor VIII mol. by said catalytic anti-factor VIII **allo-antibodies**. It also relates to an anti-factor VIII **allo-antibody**-catalyzed factor VIII degradation **inhibitor**; and to a pharmaceutical composition comprising said catalytic anti-Factor VIII **allo-antibodies** which are capable of degrading Factor VIII and which originate from said method of determination; and further to a pharmaceutical composition comprising said anti-factor VIII **allo-antibody**-catalyzed factor VIII degradation **inhibitor**. Finally, the present invention relates to the application in therapeutics of said anti-factor VIII **allo- antibody**-catalyzed factor VIII degradation **inhibitor**, of a pharmaceutical composition comprising said catalytic anti-factor VIII **allo-antibodies** which are capable of degrading factor VIII and which originate from said method of determination, and of a pharmaceutical composition comprising said anti-factor VIII **allo- antibody**-catalyzed factor VIII degradation **inhibitor**.

L12 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

2000:738600 Document No. 134:324767 Immune tolerance therapy for haemophilia. Ho, Aloysius Y. L.; Height, Susan E.; Smith, Mark P. (The Haemophilia Reference Centre, St Thomas' Hospital, London, UK). Drugs, 60(3), 547-554 (English) 2000. CODEN: DRUGAY. ISSN: 0012-6667. Publisher: Adis International Ltd..

AB A review with 69 refs. The development of anti-factor VIII and anti-factor IX **allo-antibodies** in hemophilia A and B, resp., remains a serious complication of treatment for these two X-linked hemostatic disorders, with major clin. and economic consequences. Treatment of this potentially fatal complication remains one of the greatest challenges facing hematologists at the beginning of the 21st century. Immune tolerance induction (ITI) therapy has been generally accepted as the best available treatment, extinguishing the **inhibitor** and permitting a resumption of standard dosing schedules. Although there have been several established protocols for ITI therapy developed over the last quarter century, the optimal scheme in terms of safety, clin. efficacy and pharmaco-economic considerations has yet to be determined

L12 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

1998:114393 Document No. 128:225874 Synergistic activity of malononitrilamides with cyclosporine to control and reverse xenograft rejection. Schorlemmer, H. U.; Kurrle, R. (Research Laboratories Hoechst Marion Roussel (HMR), DG-Rheumatology/Immunology, c/o Behringwerke AG, Marburg, 35001, Germany). International Journal of Tissue Reactions, 19(3/4), 149-156 (English) 1997. CODEN: IJTEDP. ISSN: 0250-0868. Publisher: Bioscience Ediprint Inc..

AB Several studies in xenotransplantation have stressed the role of humoral mechanisms of graft rejection and have emphasized the role of xenophile

antibodies as well as T-cell activation in the rejection of xenografts. Malononitrilamides (MNAs), derivs. of the primary metabolite of leflunomide, were found to be potent **inhibitors** of the IgM and IgG antibody response in vitro and were able to reduce auto- and **allo-antibody** formation in vivo. Here we tested the immunosuppressive activities of MNA 279 and MNA 715 in a concordant mouse-to-rat skin xenotransplantation model. Mouse skin xenograft survival in untreated Lewis rats (5.4 ± 1.1 days) and those given a vehicle solution only by gavage (6.1 ± 0.9 days) were statistically indistinguishable. In our model treatment with cyclosporine (10 mg/kg/day) as a single drug showed no significant prolongation of xenograft survival (6.4 ± 0.9 days) as compared to controls. When MNAs were given alone to xenograft recipients, they were able to demonstrate a significant and dose-dependent prolongation of graft survival time. Even a short-term application of these new immunosuppressive agents showed efficacy in the prevention of hyperacute xenograft rejection. Both MNA 279 and MNA 715 also have therapeutic activity and can reverse ongoing acute skin xenograft rejection. With these drugs a remarkable suppression of donor-specific IgM and IgG xenoantibody production in vivo was also clearly demonstrated by flow cytometry. Interestingly, whereas cyclosporine alone was unable to prolong xenograft survival, MNA-combination therapy, even a short-term application with an ineffective dose of CyA, was synergistically effective and significantly prolonged xenograft survival. This synergistic effect of MNAs with CyA was seen also when they were given therapeutically on days 5 to 9 and they reversed hyperacute skin xenograft rejection in this mouse-to-rat model.

L12 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

1975:123107 Document No. 82:123107 Failure of pepsin digested donor specific alloantibody to prolong renal allograft survival in dogs. Callender, C. O.; Sutherland, D. E. R.; Howard, R. J.; Toledo-Pereyra, L. H.; Najarian, J. S. (Med. Sch., Univ. Minnesota, Minneapolis, MN, USA). Immunological Communications, 3(4), 309-19 (English) 1974. CODEN: IMLCAV. ISSN: 0090-0877.

AB Donor specific F(ab')2 alloantibody fragments, prepared by pepsin digestion of IgG from hyperimmune cytotoxic alloantiserums raised in third party dogs, was administered to canine renal alloraft recipients to allow expression of immunol. enhancing properties of alloantibody in a species in which hyperacute rejection occurred. Pepsin digestion did abrogate the ability of donor specific cytotoxic alloantibody to mediate hyperacute rejection, but renal allograft survival in F(ab')2 treated dogs was not prolonged over graft survival in untreated dogs. Factors which may contribute to the inability of this technique to prolong graft survival included the difficulty, when using outbred animals, of assuring that the alloantibody was directed against all the antigens present in the donor and absent in the recipient; and the decreased potency of F(ab')2 when compared to an equivalent amount of intact IgG, as an **inhibitor** of a specific immune response.

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=> E KAVERI S/AU
=> S E3-E10
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             1 "KAVERI SIRINI"/AU
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L13        126 ("KAVERI S"/AU OR "KAVERI S V"/AU OR "KAVERI SIRINI"/AU OR "KAVE
               RI SRINI"/AU OR "KAVERI SRINI V"/AU OR "KAVERI SRINIVAS"/AU OR
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"KAVERI SRINIVAS V"/AU OR "KAVERI SRINIVAS VENKATESH"/AU)

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'SU' IS NOT A VALID FIELD CODE
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L16          30 "LACROIX S"/AU

=> E DESMAZES S/AU

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L17         359 ("KAZATCHKINE M"/AU OR "KAZATCHKINE M D"/AU OR "KAZATCHKINE
                MICHAEL D"/AU OR "KAZATCHKINE MICHEL"/AU OR "KAZATCHKINE MICHEL
                D"/AU)

=> S L13,L15,L16,L17
L18         425 (L13 OR L15 OR L16 OR L17)

=> S L18 AND (L5,L6)
L19          12 L18 AND ((L5 OR L6))

=> S L19 NOT (L10,L12)
L20           4 L19 NOT ((L10 OR L12))

=> D 1-4 CBIB ABS

L20  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
1997:124861   Document No. 126:185046  Autoantibodies which enhance the rate of
     a chemical reaction.  Paul, Sudhir; Li, Lan; Kaveri, Srini
     (Igen, Inc., USA).  U.S. US 5599538 A  19970204, 45 pp., Cont.-in-part of
     U.S. Ser. No. 259,151.  (English).  CODEN: USXXAM.  APPLICATION: US
     1994-274306 19940712.  PRIORITY: US 1989-343081 19890425; US 1991-775956
     19911025; US 1994-259151 19940613.
AB   Autoantibodies which enhance the rate of a chemical reaction of a substrate,
     processes for their preparation, their use and compns. thereof are disclosed.
     In particular, an autoantibody capable of catalyzing the hydrolysis of the
     peptide bond between amino acid residues 16 and 17 in the neurotransmitter
     vasoactive intestinal peptide (VIP) is disclosed.  Human anti-thyroglobulin
     antibodies isolated by chromatog. on protein-A and immobilized Tg hydrolyzed
     radiolabeled Tg, as shown by generation of several lower-sized products on
     SDS-electrophoresis gels.  The activity displayed a Km value of a 39 nM
     property typical of an antibody-combining site.  Tg-antibodies also hydrolyzed
     com. available peptidyl- methylcoumarinamide (MCA) substrates, displaying a
     preference for Arg-MCA and Lys-MCA containing conjugates.  The hydrolysis of
     Pro-Phe-Arg-MCA was characterized by Km (17 μM) and kcat 0.06 min-1.
     Peptidyl-MCA hydrolysis was inhibited potently by thyroglobulin (Ki 24 nM),
     suggesting a catalytic site/located in the antibody combining site.  In
     control expts., the hydrolytic activities were removed by immunoadsorption
     with immobilized anti-human IgG, and IgG depleted of the Tg-specific
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antibodies by affinity chromatog. did not display Tg and Pro-Phe-Arg-MCA hydrolyzing activities.

L20 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
1996:49440 Document No. 124:110761 **Catalytic** activity of anti-thyroglobulin **antibodies**. Li, Lan; **Kaveri, Srinivas**; Tyutyulkova, Sonia; **Kazatchkine, Michel D.**; Paul, Sudhir (Dep. of Anesthesiology and Eppley Cancer Research Inst., Univ. of Nebraska Medical Center, Omaha, NE, 68198-6830, USA). Annals of the New York Academy of Sciences, 764(Immunoglobulin Gene Expression in Development and Disease), 570-2 (English) 1995. CODEN: ANYAA9. ISSN: 0077-8923. Publisher: New York Academy of Sciences.

AB The kinetic parameters for thyroglobulin hydrolysis by catalytic anti-thyroglobulin autoantibodies obtained from a patient with Hashimoto's thyroiditis were determined The kinetic efficiency of the antibodies is derived exclusively from potent thyroglobulin binding, since the turnover rate is slow.

L20 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
1995:817161 Document No. 123:282821 Methods of measuring thyroglobulin and peptide-methylcoumarinamide hydrolysis by autoantibodies. Li, Lan; Kalaga, Ravishankar; **Kaveri, Srinivas**; Paul, Sudhir (Medical Center, University Nebraska, Omaha, NE, USA). Methods in Molecular Biology (Totowa, New Jersey), 51(Antibody Engineering Protocols), 417-21 (English) 1995. CODEN: MMBIED. ISSN: 1064-3745. Publisher: Humana.

AB A review with 7 refs. on detailed methods to measure the catalytic breakdown of thyroglobulin by autoantibody fractions. The hydrolytic specificity of the autoantibodies is determined using a panel of com. available peptide-methylcoumarinamide substrates.

L20 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
1995:467335 Document No. 122:211709 **Catalytic** activity of anti-thyroglobulin **antibodies**. Li, Lan; Paul, Sudhir; Tyutyulkova, Sonia; **Kazatchkine, Michel D.**; **Kaveri, Srinivas** (Eppley Cancer Res. Inst., Univ. Nebraska Med. Center, Omaha, 68198, USA). Journal of Immunology, 154(7), 3328-32 (English) 1995. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB Thyroglobulin (Tg)-specific autoantibodies from a patient with Hashimoto's thyroiditis hydrolyzed radiolabeled Tg, shown by production of several smaller sized products on SDS electrophoresis gels. The apparent Km value for Tg was in the nanomolar range, a property typical of an Ab combining site. The Tg antibodies also hydrolyzed tripeptide-methylcoumarinamide (MCA) substrates with lower affinity, displaying a preference for Arg-MCA and Lys-MCA containing conjugates. The hydrolysis of one of these conjugates, Pro-Phe-Arg-MCA, was inhibited competitively by Tg, suggesting a catalytic site located in the Ab combining site. In control expts., 1) the hydrolytic activities were removed by immunoadsorption with immobilized anti-human IgG; 2) IgG depleted of the Tg-specific Abs by affinity chromatog. did not display Tg and Pro-Phe-Arg-MCA hydrolyzing activities; and 3) the peptide-MCA hydrolyzing activity tracked exactly with the 150-kDa IgG peak on a gel filtration column run in denaturing solvent (6 M guanidine chloride).